

Surface-based analysis of subpial T2* signal changes at 7T in multiple sclerosis

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Introduction. The ability to detect and to classify *in vivo* gray matter (GM) lesions in multiple sclerosis (MS) is required to better understand pathological processes associated with disease progression and disability [1]. Ultra-high field magnetic resonance imaging (MRI >3T) has already shown improvements in sensitivity for detecting MS lesions in the white matter and GM using classical contrast techniques. Recently, 7T MRI enabled the detection and classification of different cortical lesion types, based on manual delineation of T2 hyperintensities [2]. To achieve a quantitative assessment of more subtle and diffuse cortical changes, we performed a surface-based analysis at a given depth from the pial surface [3], of T2*-weighted signal changes at 7T in different MS patient groups compared to age-matched healthy controls.

Methods. Acquisition. Fourteen MS patients (nine with relapsing-remitting MS, RRMS; five with secondary progressive MS, SPMS; mean±SD age=38.9±12.9 years; median Expanded Disability Status Scale=3.0, range=1.0-6.5; mean±SD disease duration=10.2±7.7 years) and eight age-matched controls were scanned twice on a human 7T Siemens scanner using an in-house developed 8- or 32-channel phased array coil, and on a 3T Siemens Tim Trio scanner using the Siemens 32-channel coil. The 7T protocol included acquisition of 2D FLASH-T2* spoiled gradient-echo weighted images (TR/TE=1000/22 ms, 20, 0.33×0.33×1mm³ slices) and a 3D MPRAGE (TR/TE/TI=2600/3.26/1100ms, 0.60×0.60×1.5 mm slices) with the same orientation as the FLASH-T2* scans. For each modality two to three slabs were acquired, allowing coverage of the supratentorial brain. During the 3T session we acquired a high- structural 3D scan with a magnetization-prepared rapid acquisition with multiple gradient echoes (MEMPR) [4] sequence resolution (0.9 x 0.9 x 0.9 mm³, T1=1200 ms, TR=2530 ms, flip angle=7°, TE=1.7+n.1.88 ms where n = 0, ..., 3, FoV=230 mm, bandwidth=651 Hz/px).

Processing. FLASH images were first corrected for B0 inhomogeneities and then normalized relative to the mean signal in the CSF. The group analysis included a two-step registration: 1) within-subject registration of 7T FLASH scans to the 3T surface of the each subject using robust boundary-based registration [5] and 2) between-subject surface-based registration of each 7T FLASH scans to a surface template, via the 3T MPRAGE. Following registration, the signal of the T2*/CSF image was smoothed (FWHM=10mm) and sampled at ~1mm deep from the pial surface. To test for significant differences between controls and all patients, patients with EDSS≥3.5 and SPMS patients, a general linear model (GLM) was performed pair-wise. An overview of the pipeline is shown in Fig 1.

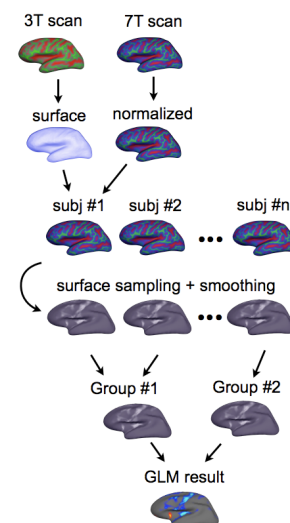


Fig 1. Processing pipeline of the surface-based analysis of cortical pathology.

Results. Registration of 7T images onto an average surface allowed performing subsequent quantifications. As an example, Fig. 2 shows an axial view of a FLASH image at 7T that has been registered onto the subject's surface. Results of the GLM analysis for the two patient groups are provided in Fig. 3 for the right hemisphere, where findings were more evident.

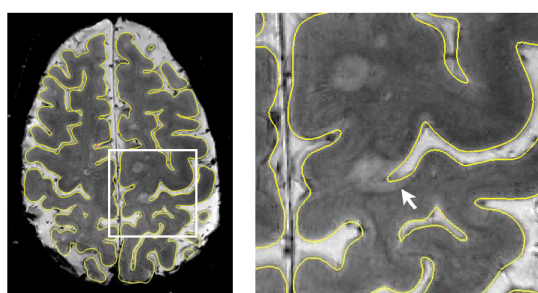


Fig 2. 7T FLASH of a patient with SPMS. The image is registered on the surface (yellow). On the zoomed panel, a cortical lesion is visible as hyperintensity (white arrow) and will be sampled on the surface for subsequent analysis.

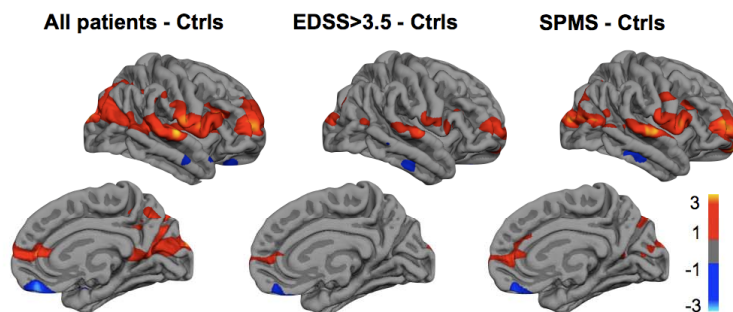


Fig 3. Overlay of the significance map on the average pial surface for the lateral (top) and medial (bottom) right hemisphere. Significant changes in T2*/CSF signal occur in the inferior parietal lobe, the superior temporal lobe, the caudal extent of the post and precentral gyri, the frontal lobe, the rostral middle frontal, superior frontal gyrus and frontal pole.

Discussion. This study reports a significant increase of the T2*/CSF signal in MS patients versus controls. This increase may reflect the diffuse subpial pathology that has been described in autopsy cases of MS. From a methodological point of view, the surface-based analysis we propose facilitates a more thorough characterization of cortical pathology *in vivo*. The combination of high field MRI, multimodal MRI and advanced processing methods has the potential to improve our understanding of the disease phenotypes via the discovery of specific biomarkers. These biomarkers are needed in order to obtain better correlations between the stage of MS and the patient's functional deficits.

References. [1] Kutzelnigg et al., J Neurol Sci 245:123-6 (2006). [2] Mainero et al., Neurology 22;73:941-8 (2009) ; [3] <http://surfer.nmr.mgh.harvard.edu/freesurfer> ; [4] van der Kouwe et al., Neuroimage 40:559-69 (2008) ; [5] Greve and Fischl, Neuroimage, 15:63:72 (2009).

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